In response to the above rejections, Applicants have amended claims 1-2 and canceled claims 3-9. In addition, new claims 17-26 are added. The amendment of claim 1 is to remove naringenin and quercetin from the list of dermal cytochrome P450 1A inhibitors and to clarify that claim 1 claims a compound, rather than a composition. New claims 17-26 seek to further clarify the meaning of the original claims 3-9. No new matter has been introduced.

Applicants respectfully submit that the amendment have overcome the objections and rejections for reasons set forth below:

Election Acknowledged

The examiner's office action states that the restriction requirement is deemed proper and therefore made final, and Applicants' election with traverse of Group 1, claims 1-9, in Paper No. 5 is acknowledged.

In this response, Applicants expressly submit that Applicants reserve any right to file continuing application(s) directing to any of the non-elected subject matter or request a reunion of the non-elected claims with the elected claims upon allowance of the subject application.

Claim Objections

Claims 3-4 and 8-9 are objected to under 37 C.F.R. §1.75(c), as being of improper dependent form for failing to further limit the subject matter of a previous claim.

Since Applicants have cancelled claims 3-9, this issue is moot.

Claim Rejections - 35 U.S.C. § 112

Claims 1-9 are rejected under 35 U.S.C. §112, second paragraph, as being indefinite.

In response to these rejections, Applicants have amended claims 1-2 and cancelled claims 3-9. Specifically, Applicants' amendment of claims 1-2 is to make clear that Applicants are claiming a compound, not a composition, which is a cytochrome P450 1A inhibitor. As described throughout the "background" section of the specification, cytochrome P450 is a group of proteins which can perform a wide spectrum of enzymatic activities including N-oxidation, sulfoxidation, epoxidation, N-, S-, and O-dealkylation, peroxidation, deamination, desulfuration, and dehalogenation. (See Specification at page 2, lines 1-3). Cytochrome P450 1A is present in human organs such as skin, intestine, and liver, and plays an important role in metabolism of highly variable molecules to affect the bioavailability of such molecules. (See Specification at page 2, lines 19-21). The cytochrome P450 1A inhibitors (i.e., CYP1A), as described in the amended claim 1, inhibit the dermal (i.e., skin) cytochrome P450 1A enzymatic activity (as claimed in claim 18).

The newly added claim 17 claims a pharmaceutical composition which comprises one or more of the free base or pharmaceutically acceptable salt of the CYP1A inhibitors. New claim 18 claims the pharmaceutical composition of claim 17 to be used in inhibiting the dermal cytochrome P450 1A enzymatic activity. New claim 19 claims the topically use of the pharmaceutical composition of claim 17 in a mammal. New claims 20-24 further limit the cytochrome P450 1A activity to a first-pass metabolism of a drug, which has been well-defined in the specification (See e.g., page 2, lines 10-16; page 3, lines 15-

21; page 7, lines 11-14). Please note that a first-pass metabolism of a drug is referred to as a drug that can be pre-maturely metabolized by CYP1A. The retinol or retinoic acid is a drug that can be prematurely degraded by CYP1A. The premature degradation of the drug decreases the usability or bioavailability of the drug. A CYP1A inhibitor inhibits the premature drug metabolism so as to prolong the life of the drug in the body. That is the reason why Applicants refer the CYP1A inhibitor as an anti-first-pass-effect compound.

Claims 25-26 further limit the cytochrome P450 1A enzymatic activity to a conversion of a chemical into a carcinogen, so as to cause, for example, skin cancer. Support of this cytochrome P450 1A enzymatic activity can be found on page 3, lines 1-14; page 9, lines 6-11; and the original claims 8-9.

Applicants respectfully request that the rejections under 35 U.S.C. § 112, second paragraph, be withdrawn in light of the cancellation of claims 3-9.

Claim Rejections - 35 U.S.C. § 102

Claims 1 and 3-9 are rejected under 35 U.S.C. §102(b) as being anticipated by the Burger reference.

In response to the rejections, Applicants have amended claims 1-2 and cancelled claims 3-9. Specifically, in the amended claim 1, naringenin and quercetin are deleted from the Markrush group. Since the Burger reference never teaches nor suggests the cytochrome P450 1A inhibitors listed in the amended claim 1, either expressly or inherently, Applicants respectfully submit that the amendment of claim 1 has overcome the anticipation rejections over the Burger Reference under 35 U.S.C. § 102(b).

In view of the foregoing, all objection and rejections have been overcome and all claims are in condition for allowance, early notice of which is requested. Should the application not be allowed, the examiner is requested to contact Applicants' attorney to resolve the issue.

Attached hereto is a marked-up version of the changes made to the claims by the current amendment. The attached page is captioned "**VERSION WITH MARKINGS TO SHOW CHANGES MADE.**"

No fee is believed to be due. Should any fee be required, please charge the same to deposit account number 22-0261 and notify Applicants' attorney.

Respectfully submitted,

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Date: March 18, 2003

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VERSION WITH MARKINGS TO SHOW CHANGES MADE

IN THE CLAIMS:

Claim 1 has been amended as follows:

Claim 1. (Once Amended). A dermal cytochrome P450 1A (CYP1A) inhibitor, wherein said dermal CYP1A inhibitor is ~~which is a free base or pharmacologically acceptable salt of at least~~ a ~~one~~ compound selected from the group consisting of (-)-epicatechin, (+)-epicatechin, (+)-limonene, 3-phenylpropyl acetate, α-naphthoflavone, apigenin, baicalein, baicalin, β-myrcene, catechin, β-naphthoflavone, cineole, daidzein, daidzin, diosmin, ergosterol, formononetin, gallic acid, genistein, glycyrrhizin, glycyrrhizic acid, hesperetin, hesperidin, isoquercitrin, kaempferol, lauryl alcohol, luteolin, luteolin-7-glycoside, ~~narigenin~~, narigin, nordihydroguaiaretic acid, oleanolic acid, paeoniflorin, ~~quercetin~~, quercitrin, rutin, swertiamarin, terpineol, trans-cinnamaldehyde, trans-cinnamic acid, umbelliferone, genkwanin, homoorientin, isovitexin, neohesperidin, wongonin, capillarisin, liquiritin, ethyl myristate, poncirin, and ursolic acid.

Claim 2 has been amended as follows:

Claim 2. (Once Amended). The dermal cytochrome P450 1A (CYP1A) inhibitor according to claim 1, wherein said dermal CYP1A inhibitor is ~~at least one~~ a compound selected from the group consisting of kaempferol, luteolin-7-glycoside, terpineol, α-naphthoflavone, β-naphthoflavone, and hesperetin.

Claims 3-9 have been cancelled.